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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/281,528	03/30/1999	DOMINIQUE ROBERTSON	5051-425	7338

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EXAMINER
KAUSHAL, SUMESH

ART UNIT	PAPER NUMBER
1636	18

DATE MAILED: 06/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/281,528	Applicant(s) ROBERTSON, DOMINIQUE
	Examiner S. Kaushal	Art Unit 1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,9,11-16,18,19,21,31,32,36-58 and 60-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,9,11-16,18,19,21,31,32,36-58 and 60-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 March 1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

ZETA ADAMS
PATENT ANALYST

DETAILED ACTION

Applicant's response filed on 01/01/01 has been acknowledged.

Claim 35 and 59 were canceled.
Claims 62-65 were newly filed.
Claims 1, 8-9, 12, 18-19, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56 were amended.
Claims 1-6, 8-9, 11-16, 18-19, 21, 31-32, 36-58 and 60-65 were pending and were examined in this office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

► *If the claims are amended, added and/or canceled in response to this office action the applicants are required to follow Amendment Practice under 37 CFR § 1.121 (http://www.uspto.gov) and A CLEAN COPY OF **ALL** PENDING CLAIMS IS REQUESTED.*

Claim Rejections - 35 USC § 112

Claims 1-6, 8-9, 11-16, 18-19, 21, 31-32, 36-58 and 60-65 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had **possession of the claimed invention** for the same reasons of record as set forth in the official action mailed on 10/11/01.

The applicant argues that the written description does not require that the application contain an exhaustive enumeration of all possible geminiviruses and transgenes. The applicant further argues that independent claims have been amended to recite "at least 80% sequence similarity" therefore it is not necessary or feasible to list all possible sequences in this context (response, page 10, ¶ 3-4). The applicant further argues that with respect to target genes the specification present working example derived from *su* and *luc* genes. The applicant further argues that one skill in the art would find that applicants to be in possession of a method of silencing any plant gene in view of results presented with *su* and *luc* genes (response, page 11, ¶ 2). The applicant further argues that the present claims recites molecule having high degree of structural similarity especially in view of written description guidelines (response, page 12). The applicant further argues that one skill in the art would recognize and appreciate that complete sequence similarity will not be required to accomplish the present invention. The applicant further argues that hybridization of shorter nucleotide sequence requires a higher degree of homology whereas lower degree of sequence homology is generally tolerated by longer sequences. Considering this applicant concluded that present invention may be practiced with recited levels of sequence similarity (response, page 13, ¶ 2). The applicant further argues that TGMV is used as an illustrative virus and the present specification states that any geminivirus may be used in view of TGMV as disclosed (response, page 13, ¶ 3). The applicant further argues that Kridl' patent only provides working examples involving construction of an African Cassava Mosiac Virus expression cassette and does not demonstrate expression of any transgene sequence therefrom but meet the written description (response, page 14, ¶ 3). The applicant concluded that invention as claimed is supported by the specification as filed.

However, this is not found persuasive because the scope of invention as claimed encompasses any and all geminivirus vectors encoding sequences capable of silencing any all genes in any and all plants species and with at least 80-95% similarity to the endogenous gene of interest. Applicant's argument alone cannot take place of evidence lacking in the record (see In re Scarbrough 182 USPQ, (CCPA) 1979). The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). At best

the specification as filed only disclosed the silencing of magnesium chelatase (su) gene and luciferase (luc) gene in N. benthamiana by particle bombardment using TGMV. The specification fails to disclose all geminivirus vectors or genomes thereof. Furthermore, the specification fails to disclose any and all hetrologous DNA sequences having at least 80-95% sequence similarity with any and all genes obtained from any and all plants. Furthermore, the specification fails to disclose that a hetrologous DNA sequences having at least 80-95% sequence similarity with any and all genes obtained from any and all plants species would silence the expression of an endogenous gene in a plant.

The earlier office action clearly states that possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention Pfaff v. Wells Electronics, Inc 48 USPQ2d 1641, 1646 (1998). In addition, one cannot describe what one has not conceived. *See Fiddes v. Baird, 30 USP2d 1481 at 1483.* In Fiddes, claims directed to a mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence (*See Fiddes v. Baird, 30 USP2d 1481 at 1483).* In instant case the specification only disclosed the silencing of magnesium chelatase gene and luciferase gene in N. benthamiana, which does not represent the genus of geminiviruses and any and all plant genes as claimed. The scope of invention as claimed encompasses any and all geminiviruses comprising any and all plant genes with 5-20% sequence variation. Furthermore, each patent application is examined on its own merit and is considered enabled in view of its own disclosure. The issue is not whether the other application support their claims but whether one supports its claims "[i]t is immaterial whether similar claims have been allowed to other" In re Gialito 188USPQ 645,648 (CCPA 1976). According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim. Therefore, the burden shifts to applicant to establish that applicants were in the possession of the claimed genus.

Claim 1-6, 8-9, 11-16, 18-19, 21, 31-32 and 35-65 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the silencing of the magnesium chelatase (su) gene and the luciferase (luc) gene in N. benthamiana using a TGMV vector, does not reasonably provide enablement for any and all geminivirus silencing vector comprising any and all geminivirus genome, a DNA construct comprising any and all geminivirus silencing vectors, wherein the genome contains hetrologous DNA which have at least 80-95% sequence similarity to any and all genes endogenous to any and all plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention **commensurate in scope** with these claims for the same reasons of record as set forth in the official action mailed on 10/11/01.

The applicant argues that working example in the present application domonstrate silencing of magnesium chelatase (su) gene and the luciferase (luc) gene in N. benthamiana with variety of different sense and antisense fragments in a TGMV derived constructs. The applicant further argues that in view of Peele, Turnage and Atkinson the constructs and methods of the present invention may be employed to silence a variety of other unrelated genes (response, page 15-16). The applicant further argues that applicant has demonstrated that claimed invention works as described in the specification accorss variety of target genes, geminiviruses, plant species and lengths of the silencing sequences. The applicant further argues that it is not possible nor is it required that applicant demonstrate silencing in all possible species, with all possible geminiviruses using all possible trangenes. All that is required is the proffered evidence representative of the claimed genus (response, page 16, ¶ 4). Considering the references cited in the earlier office action (Convey, Neuhaber and Voinnet) the applicant argues that these studies are irrelevant to the question of patentability because applicant has presented clear evidence that invention as claimed works as described in the specification (response, page 17, ¶ 2-3). The applicant further argues that using present specification as guide it would be routine for ordinary skilled worker to screen silencing fragments of different lengths in a variety of plant cells to identify the fragments that produces the desired level of gene silencing in the desired target cells (response, page 17, ¶ 4). The applicant further argues that the constructs and methods described by Voinnet are quite different from the invention as claimed, therefore are not applicable to the

invention of instant claims (response, page 18). The applicant concluded that in view of Convey and Neuhaber gene silencing of larger number of unrelated genes may be achieved with number of distantly related geminiviruses and in widely divergent plant species (response, page 19, ¶ 1).

However, this is not found persuasive because the invention as claimed encompass any and all geminivirus vectors or genome thereof, which encodes a hetrologous DNA sequence from any and all plant genes with 80-95% similarity. Applicant's argument alone cannot take place of evidence lacking in the record (see In re Scarbrough 182 USPQ, (CCPA) 1979). The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). At best the specification as filed only disclosed the silencing of magnesium chelatase gene and luciferase gene in N. benthamiana by particle bombardment. It is even unclear whether 5-20% sequence variation in nucleic acid encoding magnesium chelatase (su) gene and luciferase (luc) gene would silence the expression of respective genes in N. benthamiana. The courts have clearly stated that: "A specification did not disclose what is well known in the art. See, e.g., Hybritech Inc. V. Monoclonal Antibodies, Inc., 802 F. 2d 1367, 1385, 231 USPQ 81, 94(Fed. Cir. 1986). General off-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific material or of any of the conditions under which a process can be carried out, undue experimentation is required: there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. *It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".* Genentech Inc. V. Novo Nordisk A/s, 42 USPQ2d 1005 (CAFC 1997). It is unclear how one skill in the art would use the invention as claimed, which encompasses any and all geminiviral vectors encoding any and all plant genes, which have 80-95% similarity across any and all plant species.

The earlier office action clearly states that although gene silencing in plants as a phenomenon has long been recognized the gene silencing in plant yet incompletely understood because little is known about the relationship between nuclear and cytoplasmic events during

gene silencing (Covey et al). Furthermore, considering the unpredictability of transgene silencing in plants the understanding of the molecular basis of the invention is germane to invention as claimed. Each virus is known to produce a characteristic pattern of silencing and there are variations in the tissue specificity, which depends upon the mode of action of the suppressor and the component of gene silencing mechanism (Voinet et al, PNAS 96(24):14147-14152, 1999). Furthermore some genes escape inactivation despite the presence of a homologous partner due to subset of transformants in which both the transgene and homologous resident transgene continue to be expressed (Neuhuber et al). The invention as claimed also encompass gene silencing using episomes. The earlier office action clearly states that episomal gene silencing is not uniform in all plants and is dependent upon episomal copy number. Kjemtrup et al states that episomal gene silencing is unpredictable because to understand the relationship between episomal DNA and gene silencing, one need to determine if silencing nuclear genes could be triggered by homologous sequences carried by a geminivirus episome. Although, Kjemtrup et al provide evidence that they can down-regulate the expression of two genes in plants, they clearly state that the application of a geminvirus based vector to episomally silence a gene is a new area of endeavor.

In addition, Peele et al (The Plant J. 27(4):1-11, 2000) teaches that silencing of genes in plant varies with the tissue type and the gene of interest. For example, silencing of PCNA gene in meristematic tissue was not as uniform as loss of chlorophyll following su silencing (page 8, col.2 para.2). The invention as claimed encompass the use of a hetrologous DNA having at least 80-95% similarity, which means that 5-20% nucleotide sequences are not identical to the gene of interest. The scope of invention as claimed (claim 42-49, 62-63 and 64-65) also encompasses 80-95% sequence variation in widely divergent plant species. Therefore, it is unclear how any and all genes or variants thereof (80-95% similarity) selected from any and all plants would result in the silencing of the genes and it variants as claimed. Furthermore, geminiviruses genome has limited capacity to carry a foreign DNA sequence. For example, TGMV can carry a fragment of up to 800bp its genome to stably propagate and transcribe the gene of interest (Peele, page2, col.1 para.3). It is unclear how one skill in the art would select the minimum segment and/or its variant from the genus as claimed that would result in the silencing of the gene of interest. It is even unclear whether 5-20% sequence variation in nucleic acid encoding magnesium chelatase

(su) gene and luciferase (luc) gene would silence the expression of respective genes in N. benthamiana as exemplified in the instant specification.

In addition silencing of larger number of unrelated genes (with 80-95% sequence variation) in widely divergent plant species using any and all distantly related geminiviruses is not routine in the art and without sufficient guidance to a specific therapeutic gene the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

The amount experimentation required would include making and testing any and all gene sequences from any and all species of plants that have at least 80-95% sequence homology to any and all gene endogenous to any and all species of plant. In addition the experimentation required would further include use of DNA variants (as claimed) in silencing of any and all endogenous gene of any and all species of plants.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 9:00 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Irem Yucel can be reached on (703) 305-1998. The fax-phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Zeta Adams, whose telephone number is (703) 305-3291.

S. Kaushal
Patent examiner

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER